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Fibrous Dysplasia of Bone: Management and Outcome of 20 Cases

LUCIEN C.M. KEIJSER, MD,[1]* TONY G. VAN TIENEN, MD,[1] H.W. BART SCHREUDER, MD, PhD,[1] JOSEF A.M. LEMMENS, MD, PhD,[2] MACIEJ PRUSZCZYNSKI, MD, PhD,[3] AND RENÈ P.H. VETH, MD, PhD[1]

[1]Department of Orthopaedics, University Medical Center St. Radboud, Nijmegen, The Netherlands
[2]Department of Radiology, University Medical Center St. Radboud, Nijmegen, The Netherlands
[3]Department of Pathology, University Medical Center St. Radboud, Nijmegen, The Netherlands

Background and Objectives: Fibrous dysplasia of bone is difficult to manage because of its variable clinical course with many different methods of treatment reported. Therefore we report on our experience.

Methods: We reviewed a series of 20 patients with 32 lesions included. The average age at the time of diagnosis was 32 years for monostotic disease, 26 years for polyostotic disease, and 3 years for McCune-Albright syndrome. The median follow-up period was 6 years. Functional and radiographic outcomes were scored.

Results and Conclusions: Monostotic disease mostly presented with a circumscribed lesion and monitoring was often sufficient. Symptomatic circumscribed lesions showed satisfactory outcome when treated with curettage, cryosurgery and bone grafting. Lesions of the extended type were most of all seen in polyostotic disease and eventually needed operative treatment. In case of bony deformity, corrective osteotomies and rigid internal fixation were performed in addition to curettage, cryosurgery, and bone grafting. In polyostotic disease, expected outcomes were good, but in McCune-Albright syndrome, results were uniformly poor.

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KEY WORDS: **cryosurgery with thermocouple control; intracapsular resection; McCune-Albright syndrome; human; bone transplantation; bone diseases/developmental**

INTRODUCTION

Fibrous dysplasia of bone is characterized by immature fibrous connective tissue and poorly formed immature trabecular bone [1]. Fibrous dysplasia can compromise the structural integrity of affected bones leading to recurrent fractures and skeletal deformities. Activating mutation within the Gs gene has been described in bone cells of patients with fibrous dysplasia and in various other tissues of patients with the McCune-Albright syndrome [2–5]. This results in increased activity of the Gs protein and increased cAMP formation. Excess cAMP probably effects normal maturation of precursor osteogenic cells to normal osteoblast cells [6]. Somatic mutation of this gene early in embryogenesis could result in the mosaic population of normal and mutant-bearing tissues that may underlie the clinical manifestations of this disease.

The clinical picture of fibrous dysplasia is diverse. Its manifestation can be monostotic, polyostotic, or polyostotic in combination with skin pigmentation and dysfunction of the endocrine system (McCune-Albright syndrome) [7]. Various treatments are reported depending on age at the time of diagnosis, type and location of the lesion, and range from curettage with bone grafting to

*Correspondence to: Lucien C.M. Keijser, MD, University Medical Center St. Radboud, 800 Department of Orthopaedics, PO Box 9101, 6500 HB Nijmegen, The Netherlands. Fax No.: +31-24-3540230.
E-mail: K.Fruin@orthp.azn.nl

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massive cortical bone grafting, particular in lesions of the femoral neck and to intramedullary fixation in extended lesions with deformity [8–11]. The intent of operative treatment of the extended lesions is not eradication of the lesion but the correction or prevention of bony deformities.

Both the diversity of the disease and the multiple treatment modalities make fibrous dysplasia difficult to manage. Therefore we reviewed 20 patients and report on our experience with fibrous dysplasia in terms of treatment, tumor control, and functional outcome.

MATERIALS AND METHODS

A retrospective study was performed in 20 patients with histologically confirmed fibrous dysplasia who visited our clinic between 1992 and 1998. Thirteen patients had monostotic disease, four polyostotic disease, and three McCune-Albright syndrome. In case of polyostotic fibrous dysplasia, only symptomatic lesions of clinical significance were taken into account, though 32 lesions in 20 patients were included. There were 14 men and 6 women. The median follow-up period was 6 years (2–34). The mean age at the time of diagnosis was 32 years (12–59) for monostotic disease, 26 years (5–47) for polyostotic disease, and 3 years (2–6) for McCune-Albright syndrome. A bilateral Wilms tumor occurred in Patient 18 with McCune-Albright syndrome. Further details on primary complaints, affected bones, and medical history are listed in Table I. Fibrous lesions were operated upon if they showed a progressive deformity or an impending fracture.

Of the 32 lesions included in these series, 8 lesions were treated nonoperatively. In polyostotic disease and McCune-Albright syndrome, multiple lesions were managed nonoperatively, but these were not included because of clinical insignificance. A total of 37 pathological fractures occurred in 12 lesions during the follow-up period. All fractures were treated conservatively and no pseudarthrosis was noted. Various surgical techniques were used depending on type, location, and activity of the lesion (Table II). Symptomatic lesions were treated with curettage and bone grafting. Since 1992, cryosurgery was applied as local adjuvans using a liquid nitrogen spray (ERBOKRYO NL®, ERBE, Nieuwegein, The Netherlands) [12]. In lesions with insufficient bone stock, massive cortical allografts and internal fixation were supplemented. Corrective osteotomies with intramedullary fixation were performed in case of bony deformities. Postoperative patients were allowed to exercise with limited weight-bearing for about 3 months, regardless of the use of internal fixation.

For evaluating the outcome, the functional evaluation system of the Musculoskeletal Tumor Society was used [13]. A numerical score and percentage rate was calculated for the diseased extremity. A percentage of 70% or less was considered as an unsatisfactory result [13]. Lesions were classified on radiographs as *circumscribed* or *extended*, according to Andrisano's criteria [14]. Circumscribed lesions (Fig. 1) involve less than one-fourth of the entire bone segment and only one cortex. All other lesions are extended (Fig. 2).

When evaluating the radiographic result at follow-up examination, attention was paid to progression of the lesion or local recurrence, a pathological fracture, and a progressive deformity. With one or more of these items present, the radiographic result was considered as unsatisfactory.

RESULTS

Monostotic Disease

Five out of 13 patients with monostotic fibrous dysplasia had no complaints and because their lesions did not compromise the structural integrity of the bone, they were not further treated.

Three patients (5, 12, and 13) had an extended lesion. A progressive lesion of the femoral neck in Patient 5 was eventually treated with curettage, adjuvant cryosurgery, and bone grafting (bone chips with massive allograft) after two prior surgical procedures. Because of a localized recurrence of the lesion in the femoral neck at 5 years follow-up, the radiographic result was unsatisfactory. In Patient 12 the lesion of the proximal fibula was eventually eradicated with a marginal excision. In Patient 13 an extended lesion of the humerus was treated with curettage, adjuvant cryosurgery and bone grafting. The radiographic result was unsatisfactory due to a pathological fracture 3 years postoperatively.

Five patients had a symptomatic circumscribed lesion that was treated by curettage, adjuvant cryosurgery, and bone grafting. Except for Patient 9, the radiographic results were satisfactory. This patient, with a circumscribed lesion of the femoral neck, showed resorption of the bone graft with recurrence of the fibrous dysplasia (Fig. 1). So far, the patient is asymptomatic and no treatment is planned. Progression of a circumscribed lesion to an extended lesion was never seen in monostotic disease.

Twelve out of 13 patients with monostotic disease showed a satisfactory functional result at follow-up examination. Patient 12 was scored as unsatisfactory because of a MSTS FE score of 70% after marginal excision of the extended lesion; he suffered from modest pain, recreational restrictions, a limited walking ability, and a moderate emotional acceptance.

Polyostotic Disease

Four patients had polyostotic fibrous dysplasia with in total nine lesions of clinical significance. Curettage and

TABLE I. Clinical Data of the Group of 20 Patients With Fibrous Dysplasia*

Patient no.	Type of FD	Type of lesion	Gender	Age at the time of diagnosis (years)	Follow-up period (months)	Primary complaints	Lesions included	Site	Comments
1	M	C	F	22	24	Pain	Femoral neck	L	
2	M	C	M	22	24	Found by chance	Femoral diaphysis	L	
3	M	C	M	27	68	Swelling	Rib	R	
4	M	C	M	59	77	Pain	Proximal femoral diaphysis	L	
5	M	E	M	45	403	Pain	Femoral nech	L	
6	M	C	M	48	29	Found by chance	Rib	L	
7	M	C	M	33	25	Pain	Distal humerus	L	
8	M	C	M	35	46	Found by chance	Proximal humerus	R	
9	M	C	M	13	70	Pain	Femoral neck	R	
10	M	C	F	39	24	Found by chance	Femur (intertrochanteric)	L	
11	M	C	F	30	43	Pain	Femoral neck	R	Secondary ABC
12	M	E	M	26	399	Fracture	Fibula	R	
13	M	E	F	12	144	Fracture	Humerus	L	
14	P	E	M	47	26	Fracture	Humerus	R	Endocrine abnormalities
15a	P	C	M	5	287	—	Femoral diaphysis	L	
15b		E		5	287	Fracture	Femoral diaphysis	R	
15c		C		5	287	—	Tibial diaphysis	L	
16a	P	E	F	33	360	Pain	Total femoral involvement	L	
16b		E		33	360	—	Proximal tibia	L	
17a	P	E	F	18	259	Pain	Femoral neck	R	
17b		E		18	259	—	Proximal tibia	R	Secondary ABC
17c		C		18	259	—	Distal humerus	R	
18a	MA	E	M	2	209	—	Total femoral involvement	L	Wilms' tumor (bilateral)
18b		E		2	209	Fracture	Total femoral involvement	R	
18c		E		2	209	—	Total tibial involvement	L	
18d		E		2	209	—	Total tibial involvement	R	
19a	MA	E	M	6	156	Fracture	Proximal femur	L	
19b		E		6	156	—	Femoral neck and diaphysis	R	
20a	MA	E	M	2	288	Fracture	Total femoral involvement	L	Renal rickets
20b		E		2	288	—	Total femoral involvement	R	
20c		E		2	288	—	Total tibial involvement	L	
20d		E		2	288	—	Total humeral involvement	R	

*FD, fibrous dysplasia; M, monostotic; P, polyostotic; MA, McCune Albright syndrome; C, circumscribed lesion [14]; E, extended lesion [14]; ABC, aneurysmal bone cyst.

TABLE II. Details on Treatment of the Group of 20 Patients With Fibrous Dysplasia*

Patient no.	Latest treatment	Prior treatments	Prior treatments	Radiographic results	Functional results
1	CUR + CRYO + FG + BCG (22)			S	S
2	No treatment			S	S
3	No treatment			S	S
4	No treatment			S	S
5	CUR + CRYO + FG + BCG (45)	CUR + BCG (33)	CUR + BCG (33)	U	S
6	No treatment			S	S
7	CUR + CRYO + BCG (33)			S	S
8	CUR + CRYO + BCG (35)			S	S
9	CUR + CRYO + BCG (13)			U	S
10	No treatment			S	S
11	CUR + CRYO + BCG (30)			S	S
12	Marginal excision [26]	CUR (4)		S	U
13	CUR + CRYO + BCG (12)			U	S
14	CUR + CRYO + BCG (47)	Sling (#) (47)		S	S
15a	Cast (#) (14)			S	S
15b	PF (# diaphysis) (11)	Cast (#) (9)	NF (#) (8 and 5)	S	S
15c	No treatment			S	—
16a	CUR + megaprosthesis knee (60)	SCO (47)	ITO (33)	S	S
16b	CUR + megaprosthesis knee (60)			S	—
17a	CUR + BCG + PF [18]			S	—
17b	CUR + CRYO + FG + BCG (35)]			S	S
17c	CUR + BCG (27)			S	S
18a	CUR diaphysis + CRYO + FG + BCG (16)	O + NF (12)	Cast (#) (14, 13, 7 and 4)	U	U
18b	CUR + CRYO + O + FG + BCG + NF (16)	SCO (10)	SO (9 and 6), etc.	U	U
18c	CUR + CRYO + O + FG + BCG + NF (16)	O (12)	SO (10), etc.	S	—
18d	CUR + SO + BCG + NF (16)	SO (10)	Cast (#) (9)	U	—
19a	Marginal excision + hemi-arthroplasty (15)	ITO (8)	ITO (#) (5)	S	U
19b	CUR + CRYO + FG + BCG + NF (15)			S	S
20a	SO + FG + NF (13)	ITO (6)	Cast (#) (9, 7, 2 and 2)	U	U
20b	Cast (# diaphysis) (15)	Cast (#) (7)	ITO (6)	U	U
20c	SO + NF (11)	Cast (#) (9, 8 and 8)		U	—
20d	Cast (# diaphysis) (20)			U	U

*CUR, curettage; CRYO, cryosurgery; FG, fibula graft; BCG, bone chip graft; (), age at the time of treatment (yr); #, fracture; PF, plate fixation; NF, nail fixation; SCO, supracondylar osteotomy; ITO, intertrochanteric osteotomy; O, osteotomy; SO, Sofield osteotomy (multiple level corrective osteotomy with intramedullary nail fixation) [28].

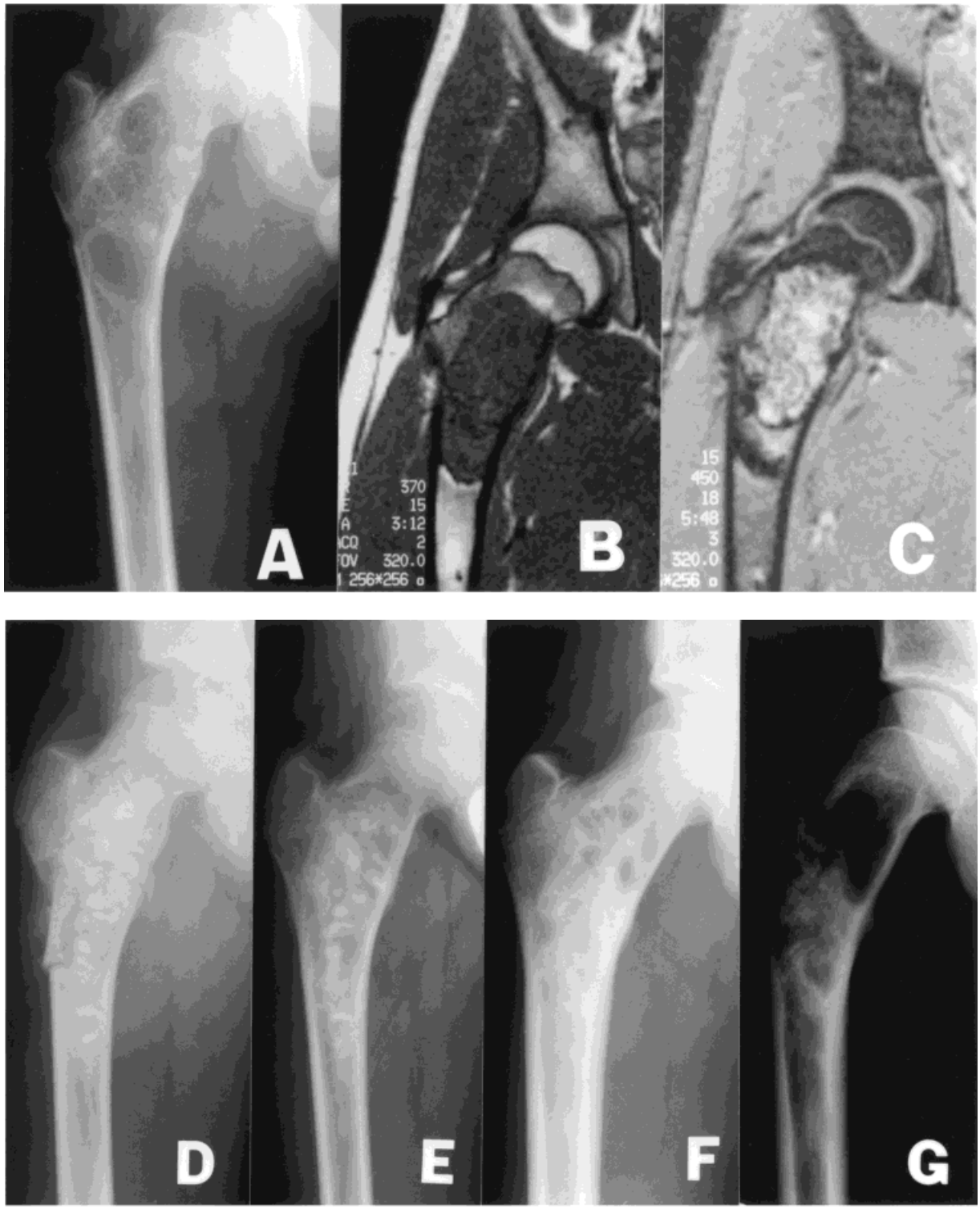

Fig. 1. Routine radiograph (**A**) of a circumscribed lesion of the right hip in Patient 9 after biopsy. Less than one-fourth of the entire femur and only the medial cortex are involved. The coronal MR images before biopsy, T1 weighted (**B**) and T2 weighted, fast spin echo sequence (**C**) show an inhomogeneous lesion without clear expansion. The postoperative follow-up is shown in (**D**) 0 month; (**E**) 6 months; (**F**) 24 months; and (**G**) 60 months. There is a gradual resorption of the bone graft but with a recurrence of the fibrous dysplasia in the femoral neck. So far the patient is asymptomatic and no treatment is planned.

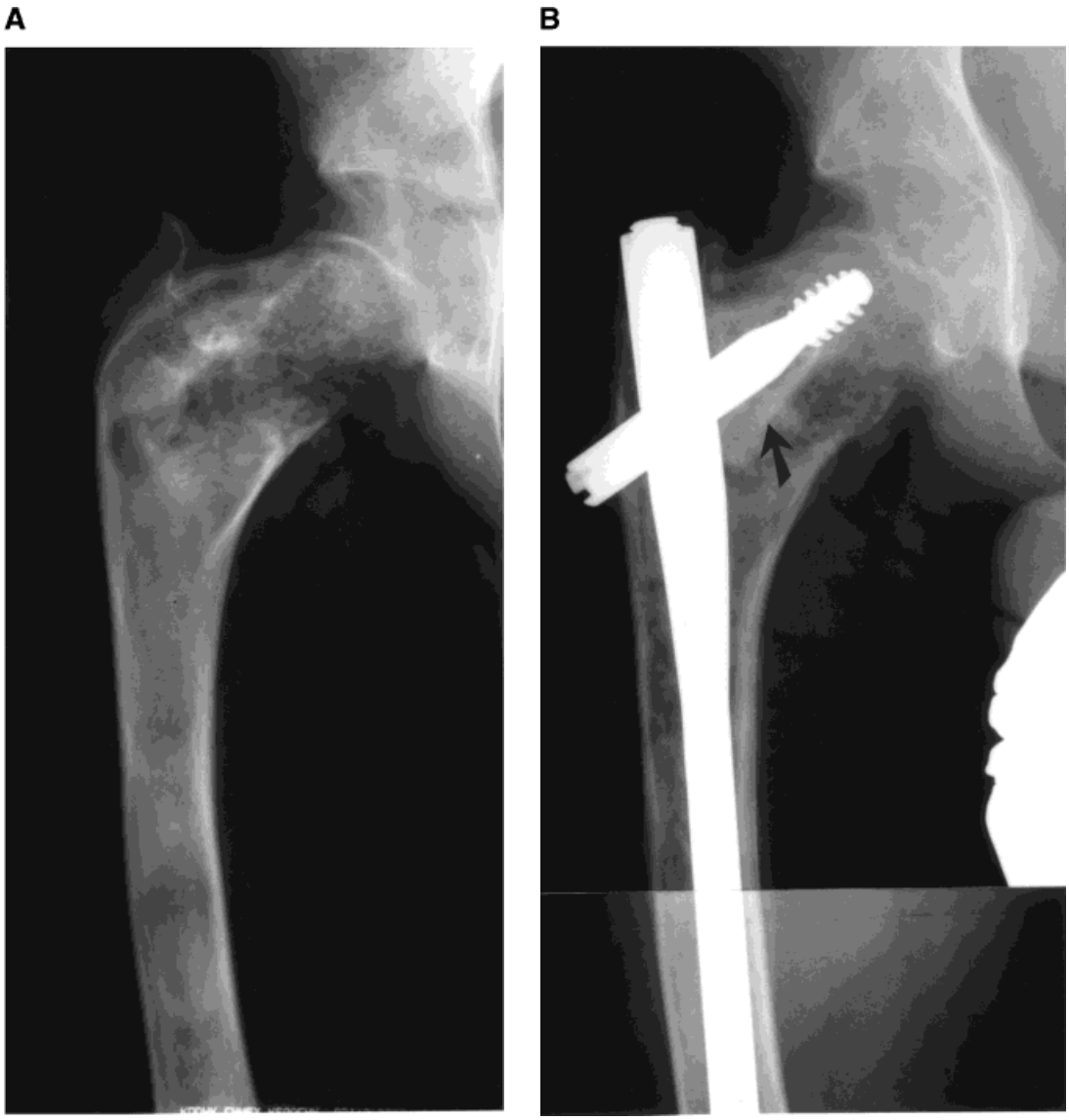

Fig. 2. Routine radiograph (**A**) of an extended lesion of the right proximal femur in Patient 19. There is involvement of more than one-fourth of the entire femur and both cortices with a slight varus deformity. An osteolytic lesion of the femoral neck and multiple endosteal erosions are present. The postoperative follow-up is shown in (**B**) 10 weeks and (**C**) 3 years. After curettage, cryosurgery and bone grafting the lesion is augmented with an intramedullary nail and a massive fibular allograft (arrow). Improvement of the bone stock during follow-up.

bone grafting with or without adjuvant cryosurgery was performed in three lesions. In two lesions loss of bone stock necessitated additional rigid internal fixation and in one patient two adjacent periarticular lesions were treated with a megaprosthesis. Two lesions were not treated operatively.

Three out of nine lesions were of the circumscribed type. Two circumscribed lesions were just monitored and one was treated with curettage and bone grafting. The six extended lesions needed operative treatment in all cases, sometimes with multiple procedures to deal with a recurrent fracture and deformity. All the lesions in polyostotic disease had a satisfactory radiographic result. All the patients with polyostotic fibrous dysplasia showed a satisfactory functional outcome.

McCune-Albright Syndrome

Three patients with 10 extended lesions of clinical significance were diagnosed as McCune-Albright syn-

C

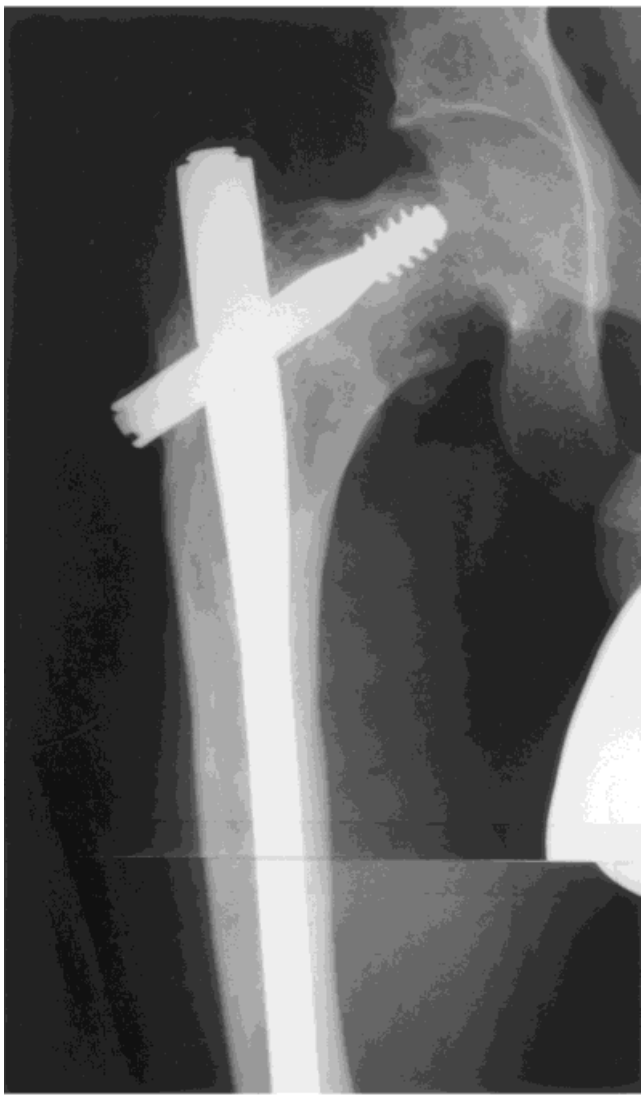

Fig. 2. (*Continued*)

drome. Symptoms presented at the age of 2–6 years. All patients were repeatedly treated with corrective osteotomies and intramedullary fixation for the management of aggressive progression of the disease throughout the follow-up period. In Patient 18 an attempt was made to correct the shepherd crook deformity; the procedure was aborted because of massive blood loss during exposure of the proximal femur. Patients 18 and 20 were treated with bisphosphonates in an attempt to modify the aggressive behavior of the disease. No response could be observed.

Seven lesions demonstrated progress of the deformity and an unsatisfactory radiographic result at the time of follow-up. Patients 18 and 20 developed a shepherd crook deformity of the bilateral proximal femur at the time of follow-up examination. In lesion number 18c, 19a, and 19b the radiographic result was satisfactory. The result of lesion 19b is shown in Figure 2. In only 2 out of 10 lesions (19b and 20d) the functional outcome was satisfactory.

DISCUSSION

The first symptoms of fibrous dysplasia are usually noted between 5 and 20 years of age; the more extended the disease, the earlier the onset of symptoms [15]. It is believed that fibrous dysplasia loses its potential to proliferate at the end of growth of the patient and matures into fibro-osseous tissue [9,14–18]. In our series, however, 13 patients presented after the age of 20 years.

The importance of age at the time of diagnosis regarding treatment has been emphasized [1]. Those lesions that showed an impending fracture or a progressive deformity were operated upon in these series, regardless of age. All the other lesions were managed non-operatively. In general, lesions that presented at an early age were biologically aggressive leading to bony deformities that needed surgical treatment.

Nonsurgical treatment with bisphosphonates is an option for those patients with generalized skeletal involvement. Preliminary studies report relief of pain and regression of fibrous lesions with intravenous infusions of pamidronate [19,20]. In our series, two patients with McCune-Albright syndrome have been treated with bisphosphonates without a beneficial effect on the course of the disease.

In this series, monostotic fibrous dysplasia was usually associated with circumscribed type lesions and when this was the case, the fibrous dysplasia was minimally aggressive, lesions did not give rise to bony deformities, and monitoring was often sufficient. When operative treatment is performed, a single procedure of curettage, cryosurgery, and bone grafting without additional internal fixation is sufficient. A satisfactory functional outcome is the rule; we encountered three local recurrences on radiographic examination in lesions that were all of the extended type.

In contrast to our experience, studies on curettage and bone grafting of *monostotic* fibrous dysplasia report negative results attributed to incomplete removal of the fibrous tissue and subsequent replacement of the graft by dysplastic bone (Table III) [9,11,14,21]. Whether or not these lesions are of the circumscribed type is not specified. The benefit of adjuvant cryosurgery in the treatment of monostotic fibrous dysplasia remains the question, for we did not perform a controlled trial. We apply cryosurgery as local adjuvant therapy to intrale-

TABLE III. Details of Studies on Fibrous Dysplasia

Author	Type of FD	No. of patients	Age (y)	Follow-up period (y)	Conservative treatment	Curettage	Curettage + bone graft	Curettage + bone graft + cryosurgery	Cortical bone graft	Internal fixation	Corrective osteotomy	En bloc excision
Stephenson '87	M	43	15	10	12 (5)	1 (0)	23 (13)	—	—	7 (1)	—	3 (0)
	P	—	—	—	48 (25)	—	18 (14)	—	—	16 (2)	—	3 (1)
Döhler '86	M	4	40	8	—	3 (0)	1 (0)	—	—	—	—	—
	P	9	8	10	2 (0)	—	—	—	—	4 (1)	6 (3)	—
Henry '69	M	28	?	12	—	—	24 (9)	—	—	—	—	4 (0)
	P	—	—	—	—	—	—	—	—	—	—	—
Harris '62	M	13	21	16	4 (0)	—	11 (5)	—	—	—	—	9 (1)
	P	37	13	24	—	—	—	—	—	7 (3)	11 (9)	—
Stewart '62	M	16	18	5	1 (1)	2 (1)	12 (1)	—	—	2 (?)	1 (1)	1 (0)
	P	4	9	15	2 (1)	1 (1)	3 (2)	—	—	1 (?)	—	—
Nakashima '84	M	8	21	9	—	—	7 (1)	—	—	—	—	1 (1)
	P	—	—	—	—	—	—	—	—	—	—	—
Andrisano '91	C	37	9	7	—	38 (22)	—	—	—	—	—	2 (1)
	E	28	9	7	—	45 (45)	—	—	—	31 (31)RIF 8 (2)IN	—	—
Enneking '86	M	10	18	7	—	—	—	—	10 (2)	—	—	—
	P	23	5	6	—	—	—	—	5 (0)	—	—	—
Guille '98	M	9	9	14	11 (11)	—	9 (5)	—	1 (0)	—	5 (1)	—
	P	8	13	15	21 (13)	—	9 (6)	—	—	1 (1)	16 (11)	—
Keijser	M	13			5 (0)	—	—	7 (3)	—	—	—	1 (1)
	P	7			3 (1)	—	1 (0)	4 (1)	—	2 (0)	6 (6)	3 (2)
Total		297			109 (57)	90 (69)	118 (56)	11 (4)	16 (2)	79 (41)	45 (31)	27 (7)

(), number of poor results according to the author's description; RIF, rigid internal fixation; IN, intramedullary nailing, M, monostotic; P, polyostotic; C, circumscribed lesion [14]; E, extended lesion [14].

sional resection because of its favorable results in reduction of the local recurrence rate of benign and low-grade malignant bone tumors [22–27].

Polyostotic fibrous dysplasia presented most commonly with extended lesions, while lesions in McCune-Albright syndrome were all of the extended type. Marked progression of the disease is seen in those cases that presented before the age of 10 years, supporting the relation between age of onset and biological aggressiveness [21]. Most extended lesions in *polyostotic* disease sustained multiple pathological fractures and multiple operative procedures focused on prevention or correction of bony deformities. Both functional outcome and radiographic result show favorable results in extended lesions in polyostotic disease. Extended lesions in McCune-Albright syndrome tend to progress despite all efforts, however, including the local adjuvant cryosurgery, resulting in poor functional and radiographic outcome.

Concerning the treatment of progressive extended lesions in polyostotic disease, there is agreement about the disappointing results of curettage and bone grafting. The early treatment with corrective osteotomies and rigid internal fixation to prevent bony deformities is emphasized [10,11,14,15]. Enneking suggested the use of massive cortical allografts to supplement dysplastic bone on condition that an existing deformity is corrected and internally fixated [1]. Studies on fibrous dysplasia report variable expected outcomes in polyostotic disease probably due to the diversity of the patient groups (Table III). Such a marked difference in expected outcome as we found between polyostotic fibrous dysplasia and McCune-Albright syndrome has not been demonstrated before.

CONCLUSIONS

It is our experience, in contrast to earlier reports, that fibrous dysplasia usually presents after the age of 20 years. Circumscribed lesions of fibrous dysplasia, most of them part of monostotic disease, are not likely to progress. When complaints arise, operative treatment with curettage, cryosurgery, and bone grafting shows a satisfactory outcome. Extended lesions may result in bony deficiency or deformities necessitating additional internal fixation, massive allografts, or corrective osteotomies. In our series, functional outcomes of extended lesions in monostotic and polyostotic disease are satisfactory, although some lesions need multiple operative procedures. On the other hand, extended lesions in McCune-Albright syndrome result in poor clinical outcomes. We continue the use of cryosurgery in the treatment of fibrous dysplasia because of its favorable results, though this can not be stated by controlled studies.

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